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ARTICLE TYPE

Determining hydrogen positions in crystal engineered organic molecular complexes by joint neutron powder and single crystal X-ray diffraction**Marc Schmidtman^a, Paul Coster^b, Paul F. Henry^c, Valeska P. Ting^d, Mark T. Weller^e and Chick C. Wilson^{e,*}**⁵ Received (in XXX, XXX) Xth XXXXXXXXX 20XX, Accepted Xth XXXXXXXXX 20XX

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The potential of neutron powder diffraction (NPD) to provide vital information on the determination of accurate hydrogen positions in organic molecular crystals is demonstrated through the study of a series of hydrogen bonded molecular complexes with relevance in crystal engineering. By studying complexes designed to contain short, strong hydrogen bonds, the findings are shown to be of particular importance in the study of proton transfer, and the often critical distinction between neutral complexes and salts in these molecular materials. The use of combined NPD and single crystal X-ray diffraction is shown to be particularly potent in this area.

The method of choice to determine accurate hydrogen atom parameters in crystalline materials is single crystal neutron diffraction (SCND). Growing single crystals of sufficient size, however, is non-trivial and often impossible, leaving neutron powder diffraction (NPD) as an alternative to probe for the nuclear densities of light atoms. The disadvantages of NPD are the massive reduction of information inherent to powder diffraction, which limits the complexity of the material for which atomic resolution can be achieved, and the very high backgrounds in NPD patterns caused by the presence of the naturally abundant ¹H isotope due to its large incoherent scattering cross section, $\sigma_{\text{inc}} = 80.27$ barns (about 50 times its coherent scattering cross section, $\sigma_{\text{coh}} = 1.76$ barns). This results in poor counting statistics for even very long counting times, and in consequence, NPD was long perceived as unsuitable for the structure determination of materials containing significant amounts of ¹H, and deuteration as a requirement to reduce the incoherent scattering in such cases ($\sigma_{\text{inc}}(^2\text{H}) = 2.05$ barns). Recent advances in neutron instrumentation, i.e. increased neutron flux on the sample and improved neutron detection in terms of detector efficiency and detector coverage, and the consequential reduction in counting times, have changed the above view considerably and an increasing number of hydrogen-containing materials have been successfully characterised by NPD¹.

To date, little attention has been focused on the applicability of NPD towards the structure determination of organic structures, partly accounted for by the fact that, given a reasonable data quality, single crystal X-ray diffraction (SCXD) experiments routinely provide hydrogen atom parameters in organic materials. However, these H-atom parameters are affected by systematic

errors and covalent X–H distances are artificially shortened due to electron transfer from hydrogen into the covalent bonds. This is well understood² and can in many compounds be countered by ‘normalisation to neutron distances’ by setting X–H distances to reference distances obtained from accurate SCND experiments.

There are situations, however, when such a normalisation is neither desirable nor appropriate, for instance when the H-atom in question is involved in (strong) hydrogen bonding, resulting in considerable elongation of the X–H bond, and the ‘true’ X–H and H...Y distances are used as measures of the hydrogen bond strength. Furthermore, in the extreme case of short, strong hydrogen bonds (SSHBs), additional charge transfer effects result in strong electron density delocalisation (further depletion of the hydrogen atom density and overlap with bonding density from donor and acceptor atoms) and can considerably complicate the localisation of H when based on even high resolution SCXD. Such systems are important in several contexts – they are an important means of potential charge transfer effects, can have a significant effect on solid-state properties, and can be exploited in the area of crystal engineering, as they represent an often predictable and repeatable hydrogen bonding motif. To understand fully such ‘unusual’ H-atoms, and their effect on structure and properties, requires probing by neutrons; this work addresses what and how much information NPD can add to SCXD experiments in terms of determining accurate H-positions in organic structures. The joint use of NPD and SCXD has also been probed in inorganic and organometallic systems, including our own systematic previous studies¹ and other recent work³.

While the study of materials with SSHBs using PND following deuteration to reduce the level of incoherent scattering and improve data quality can be envisaged, such work is normally extremely time-consuming and in many cases practically impossible. Furthermore, deuteration of SSHBs markedly affects the properties and strengths of hydrogen bonds⁴ and in some cases leads to a different solid state structure for the compound^{5,6}. However, where the ¹H and ²D compound structures remain the same the additional possibility exists to study directly the effect of deuteration on the nature of the hydrogen-bond.

The materials investigated here belong to the class of (strongly) hydrogen bonded molecular co-crystals and salts⁷ (Figure 1): the 1:1 complexes of pentachlorophenol with 2,6-dimethylpyridine **1** and 2,4-dimethylpyridine **2**⁸; the two polymorphic 2:1 complexes of isonicotinamide with oxalic acid

3-I, **3-II**⁹ and its partially deuterated isotopomeric form **3d**; and the 1:1 complex of 3,5-dinitrobenzoic acid with 4-methylpyridine **4**¹⁰ and its partially deuterated analogue **4d**. All samples were prepared by simple solvent evaporation in solvent systems as described in previous studies of these materials. For natural

isotope (hydrogenous) materials, evaporative crystallisation was carried out in an environment open to the atmosphere, while for some of the deuterated samples, evaporations took place (from deuterated solvent) within a large sealed vessel, initially purged of water vapour (see below).

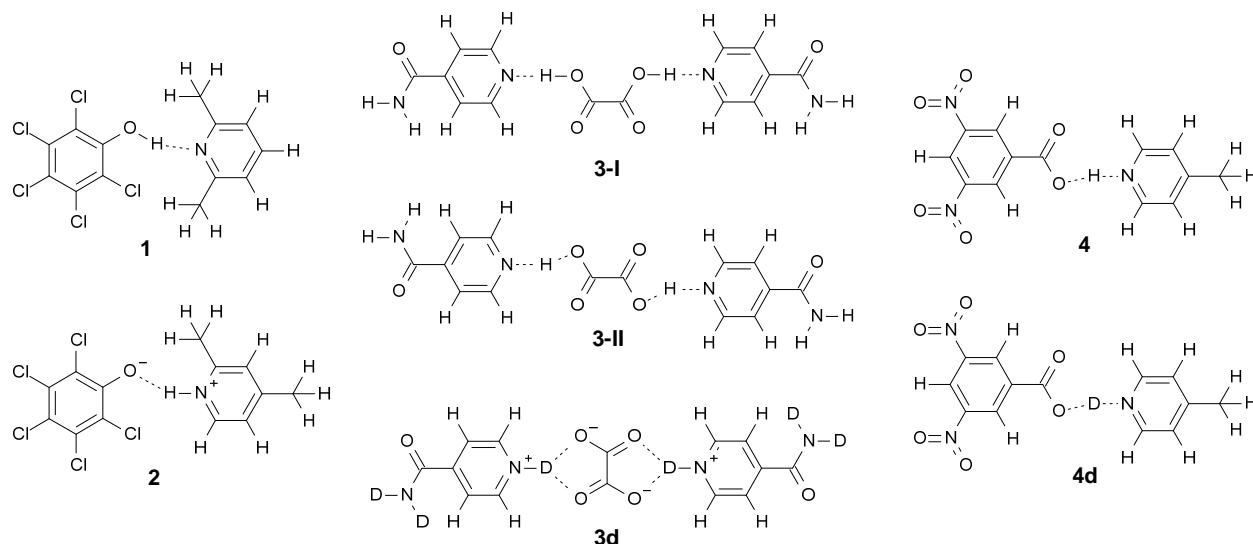


Fig.1 Molecular complexes **1-4d**

F

NPD data of **1-4** were collected on D20 at the ILL, Grenoble¹¹, at a single wavelength of 1.87Å. D20 is a high flux diffractometer in close proximity to the neutron reactor and has a large detector covering 160° allowing for fast data collections (60-120 minutes per dataset in this study), but has the disadvantage of a comparatively low spatial resolution (0.1° per detector cell). Powdered samples of (0.5-1.0g) **1-4** were loaded in vanadium cans, and cooled to 100K to match the SCXD data collection temperatures. NPD was combined with SCXD in joint structure refinements, using two complementary and, from the experimental point of view, two routine techniques. During the refinements the heavy atom parameters (in this context C, N, O) should be dominated by the SCXD data and the H parameters by the NPD data. The inclusion of SCXD data has the benefit of replacing rigid body models for the organic molecules which would be required otherwise because powder diffraction (X-ray or neutron) on its own does not provide sufficient data for individual atom refinements of the comparatively complex organic structures studied here (19-33 independent atoms).

All atomic parameters (fractional coordinates and anisotropic atomic displacement parameters (ADPs)) were refined simultaneously against the NPD and SCXD data with Topas Academic¹¹ (see Figures S1-S8 in ESI[†]) without the use of restraints or constraints, other than that the H isotropic ADPs were kept equal in each structure. Discussion of these previously determined structures focuses here on the added information obtained on the important hydrogen atoms by the use of NPD data, rather than in structural descriptions that are available in the previous literature. The refined H positional parameters are benchmarked against SCND data where available (ESI, Tables S1

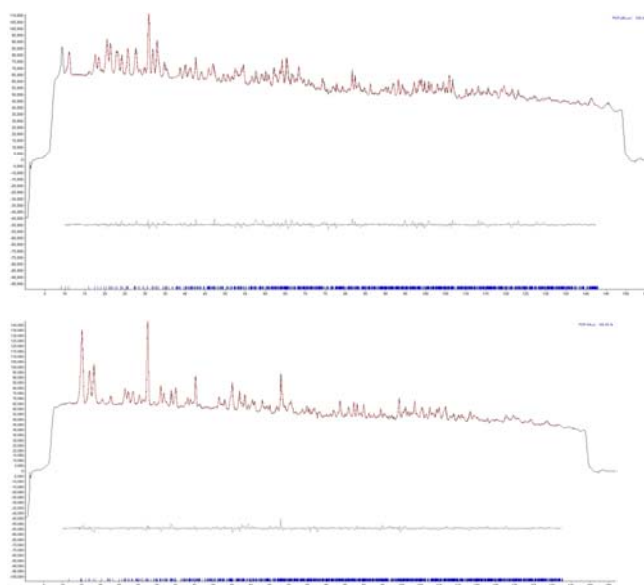


Fig. 2 Final Rietveld fits for complexes **1** and **2**, illustrating the high background levels in NPD of hydrogenous molecular complex materials.

and S2), and also against C–H bond lengths derived from the SCND data deposited in the Cambridge Structural Database (CSD)¹³.

As a first test, the 1:1 pentachlorophenol–dimethylpyridine complexes **1** and **2** were chosen to test the applicability of NPD for the distinction between a ‘neutral’ molecular complex (co-crystal) and a ‘charged’ H transfer complex (salt). The H atoms in question are situated in comparatively strong O···H···N HBs

linking the phenol and the pyridine base. The H content of 33 atom% in **1** and **2** results in the aforementioned high background in the NPD patterns as shown in Figure 2 for the final profile fits of the Rietveld refinements. Furthermore, the peak overlap is already significant despite the relatively simple structures with one formula unit per asymmetric unit and unit cell volumes of $\sim 740 \text{ \AA}^3$ ($P\bar{1}$) and 1480 \AA^3 ($P2_1/n$) for **1** and **2** respectively. According to earlier SCXD experiments⁸, **1** constitutes a co-crystal and **2** a salt with O–H and N–H bond lengths refining to 0.88(2) and 0.90(2) Å respectively. The joint NPD + SCXD structure refinements confirm these protonation states but yield O–H and N–H bond lengths of 1.082(16) and 1.063(16) Å respectively, which is in much improved agreement with the nuclear geometries expected for such HBs. It is also evident that the NPD data are largely accountable for the determination of the H positions in these joint structure refinements. The effect on the numerous C–H bonds is discussed below.

The polymorphic 2:1 complexes isonicotinamide – oxalic acid **3-I** and **3-II** exhibit ‘unusual’ H atoms in nearly centred and centred $\text{O}\cdots\text{H}\cdots\text{N}$ SSHBs respectively. Deuteration of **3** leads to the formation of an isotopomeric⁶ polymorph **3d**¹⁴, implying that **3-I** and **3-II** can only be studied in their ‘natural’ forms, that deuteration as a way to avoid the incoherent scattering of ^1H is not an option in this case. For both polymorphs accurate H parameters are available from SCND experiments¹⁵ and this material therefore constitutes an ideal candidate to test the accuracy of NPD. The NPD + SCXD refinements result in O–H distances of 1.179(18) and 1.253(15) Å in the SSHBs of **3-I** and **3-II** respectively, which is in excellent agreement with the SCND derived values of 1.161(3) and 1.235(5) Å respectively.

Neutron diffraction has the additional advantage of being capable of distinguishing between isotopes, i.e. between H and D in case of **3d**. NPD should, therefore, allow an easy quantification of the deuteration levels and the distribution of H/D atoms in the structure. **3d** has been obtained by crystallisation from D_2O in open (allowing H/D exchange with the atmosphere) and closed conditions. Refinement against the NPD data reveal that, as expected, only the carboxylic acid and amide H atoms have been subject to isotope exchange. Here, the deuteration levels refine to approximately 70% (oxalic acid O–D) and 80% (amide N–D) in case of the open crystallisation experiment, while complete deuteration was achieved during the experiment conducted in closed conditions. The effect of sample deuteration is also reflected by the drop of the background levels in the NPD patterns as the H content decreases from 37 atom% in **3** to 21 atom% in **3d** (Figures S3, S6; ESI).

The molecular complex of 3,5-dinitrobenzoic acid with 4-methylpyridine **4** is another example of a material exhibiting an unusual $\text{O}\cdots\text{H}\cdots\text{N}$ SSHB. According to the room temperature SCXD study¹⁰ the H atom occupies a centred position in the SSHB with O–H and N–H distances of 1.261(17) and 1.267(17) Å respectively; the structure deposited in the CSD (REFCODE DAKWES), however, has been refined with the H atom disordered over two sites, indicating a mixture of a neutral and a charged complex. In order to clarify this matter, **4** and also its deuterated analogue **4d** were re-investigated by SCXD and NPD at 100K. Refinement against the NPD data reveals a single

site for the H atom in **4**, centred in the SSHB, and the O–H and N–H distances of 1.28(2) and 1.264(19) Å respectively correspond well to those of the original room temperature SCXD study. Exchanging the benzoic acid H for D results in an isostructural complex (80% deuteration level with respect to the benzoic acid O–D) but the D atom in the SSHB is shifted slightly towards the pyridine base with O–D and N–D bond lengths refining to 1.339(15) and 1.201(14) Å respectively. Also, SCXD experiments at 100K reveal single sites for the H and D atoms, but the electron densities are considerably elongated in the direction of the HB path and the H/D atoms refine to positions slightly closer to the pyridine base (N–H = 1.19(2) and N–D = 1.125(18) Å), again highlighting the fundamental difference between nuclear geometry and electron density maxima. The difference between N–H and N–D distances in this case may also represent a small but significant isotope effect.

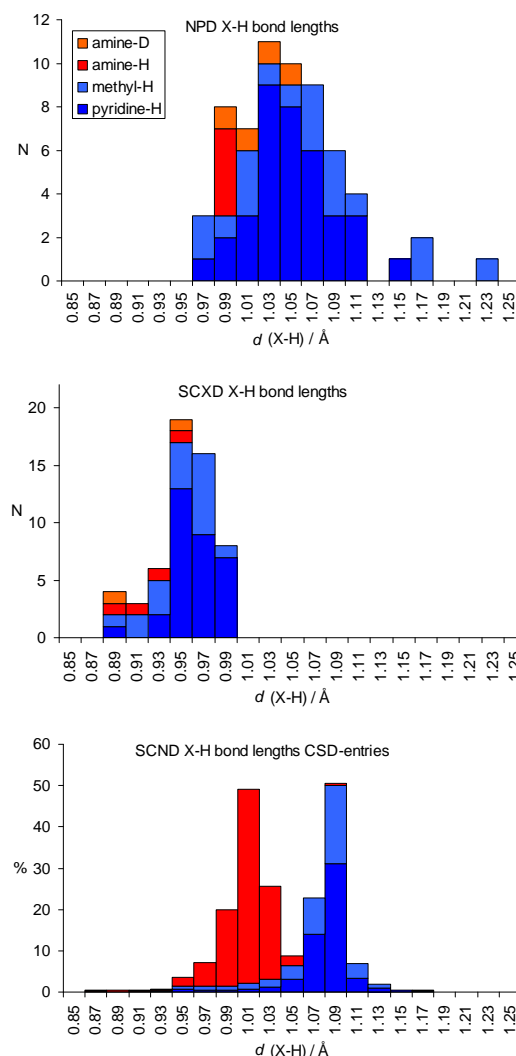


Fig. 3 C–H and N–H(D) bond lengths in **1–4** as refined from NPD and SCXD, for comparison neutron bond lengths from the SCND entries in the CSD.

In order to assess the accuracy of the H determination, the distribution of C–H bond lengths obtained from the NPD + SCXD refinements can be compared against the average C–H bond length of 1.076 Å obtained from the SCND entries deposited in the CSD. For this purpose, all C–H bond lengths are assumed to be the same, for the marginal variations that can be detected by SCND studies are inaccessible by powder diffraction. Figure 3 shows the distributions of NPD and SCXD derived C–H (and N–H) bond lengths in **1–4** in comparison with the corresponding distribution obtained from the CSD SCND entries. The NPD C–H distances are on average ~0.1 Å longer compared to the SCXD (average C–H_{NPD} = 1.056, C–H_{SCXD} = 0.958 Å) which corresponds approximately to the expected systematic differences between the two methods. NPD therefore yields accurate values considerably closer to the nuclear C–H bond distance of ~1.08 Å than SCXD, and the H positions are clearly dominated by the NPD data during the joint structure refinements. On the other hand, the individual NPD distances are spread over a comparatively large range (0.97–1.22 Å) and thus lack, naturally, the precision which can be achieved by SCND. Furthermore, a differentiation between pyridine and methyl H in Figure 2 shows that the spreading is pronounced for the methyl C–H which suffer from stronger thermal displacements, whilst the pyridine C–H (and amide N–H) bond lengths show tighter distributions about the average.

Conclusions

In conclusion, NPD can be seen to provide a tool that assists in the localisation and refinement of H atoms in organic structures. The joint NPD + SCXD structure refinements increase the accuracy of H positional parameters compared to refinements against SCXD data only. They also add confidence to the localisation of ‘unusual’ H atoms in, for example, strongly hydrogen bonded systems, as nuclear densities are probed rather than the diffuse H electron densities. This also allows investigation of the differences between H and D in their hydrogen bonding behaviours. Here, we have found a remarkably good agreement in accuracy between the joint NPD + SCXD studies and SCND. On a negative note, the distribution of C–H distances clearly exhibits a lack of precision in NPD derived H parameters. However, it is important to note that in this case the desired atomic resolution in these organic materials is sought, for the H atoms specifically, essentially through individual atom refinements against the powder data. On a final note, it is important to stress that NPD can act as a powerful alternative to SCND in cases where SCXD does not provide sufficient information on H atoms and SCND is not an option. NPD cannot replace SCND where crystals of sufficient size exist and sufficient beam time is available. However, given the relatively short timescales required to obtain NPD data, 60–120 mins in this study, compared with, typically, 1–3 days for SND work, NPD has a clear role to play in the study of some systems. For example where evolution of selected structural parameters as a function of sample environment, such as temperature, pressure or humidity, is of interest¹, NPD can provide such data on reasonable experimental timescales of a day or less while SND studies, albeit at much higher precision, might take weeks.

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Notes and references

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- [†] Electronic Supplementary Information (ESI) available: Final Rietveld fits for all neutron powder diffraction data, Tables of bond distances involving H atoms. See DOI: 10.1039/b000000x/
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